PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
IB/G-33653A/BCK		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/001378	11.02.2004	13.02.2004

International Patent Classification (IPC) or national classification and IPC
INV. C07D417/12 A61K31/4439 A61P3/10 C07D277/00

Applicant
SANDOZ AG

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in celectronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16.11.2005	09.05.2006

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Seymour, L

Telephone No. +49 89 2399-8694

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2005/001378

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-41 as originally filed

Claims, Numbers

1-36 as originally filed

Drawings, Sheets

1/11-11/11 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2005/001378

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 35 and 36 with respect to industrial applicability

because:

☒ the said international application, or the said claims Nos. as above relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2005/001378

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-20,24-30
	No:	Claims	1,21-23,31-36
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-36
Industrial applicability (IA)	Yes:	Claims	1-34
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Re Item III

Claims 35 and 36 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

1. Reference is made to the following documents:

   D1: WO 03/050113 A D2: US-B1-6 329 403 D3: WO 94/05659 A

2. It is maintained that the present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1, 21-23 and 31-36 is not new in the sense of Article 33(2) PCT:

   The applicant argues that the present claims are novel over D2 since this document does not specifically disclose the phosphoric acid salt form of rosiglitazone, but only discloses a pharmaceutical composition comprising an insulin sensitizer which may be, among many others, rosiglitazone or a salt thereof, whereby one of many possible salt forms listed is phosphoric acid.

   The examiner cannot agree with this assessment of the disclosure of D2. In claims 8, 9, 12, 13, 16 and 17, D2 singles out "rosiglitazone or a salt thereof" for use in the invention disclosed. The possible salts envisaged are listed in column 9, lin 66 - column 10, line 26, one of which is phosphoric acid (column 10, line 13). The combination of rosiglitazone with phosphoric acid results from the choice within a single list. No selection of multiple variables is required. The disclosure in D2 inevitably leads the skilled person to the salts of rosiglitazone listed, including the salt with phosphoric acid. Novelty must therefore be denied.

   The use of compositions thereof for treating diabetes mellitus is also disclosed (column 11, lines 49-57).

The remaining claims directed to rosiglitazone phosphate having a molar ratio of 1:1 and polymorphs thereof are considered to be novel since D1-D3 do not disclose the phosphate salt with said stoichiometry.

3. It is maintained that the present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of the present claims does not involve an inventive step in the sense of Article 33(3) PCT.

According to the present description (page 1, paragraph 4), the problem underlying the present application lies in the provision of alternative salt forms of rosiglitazone which are straightforward to prepare and which have properties suitable for pharmaceutical processing on a commercial scale.

Document D1 is regarded as being the closest prior art because it discloses a salt of rosiglitazone with an inorganic polybasic acid, namely sulfuric acid, in the same stoichiometry as the present salts (1:1). In addition, as pointed out by the applicant, this salt solves the above-mentioned problem (page 1, lines 13 to 14 and page 2, line 33 to line 36).

Phosphoric acid is a well-known counterion for pharmaceutical salts and is furthermore suggested as a favourable pharmaceutical salt in D2 as next in the list after sulfuric acid (see column 10, lines 12-13). The formation of the phosphate is therefore considered to be a straightforward possibility for the skilled person to select when faced with the above-mentioned problem. The examiner cannot accept the applicant's argument that the skilled person would not look into D2, because D2 is directed to solve a completely different technical problem. The skilled person would consider any document in which salts of rosiglitazone are used within a pharmaceutical context. In any case, as stated above, it is considered to be general knowledge that phosphoric acid is a suitable counterion for pharmaceutical salts.

An inventive step cannot therefore be acknowledged, in the absence of evidence showing an unexpected advantage with respect to the structurally closest prior art salt, i.e. rosiglitazone hydrogensulfate. The present application does not provide any evidence of unexpectedly favourable physico-chemical properties with respect to this known salt of the prior art.

4. For the assessment of the present claims 35 and 36 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 2005/023803 A (D4)	17.03.2005	10.09.2003	

D4 discloses rosiglitazone phosphate having a molar ratio of 1:1 (see claim 1) and the use thereof in treating diabetes (p. 1, line 30 - p. 2, line 11).